201-14938

Anh Nguyen
12/22/03 08:49 AM

To: NCIC HPV@EPA
cc:
Subject: HPV Robust Summaries/Test Plan

----- Forwarded by Anh Nguyen/DC/USEPA/US on 12/22/2003 08:46 AM -----

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12/19/2003 02:53 PM

To: NCIC OPPT@EPA, hpv.crtk@epamail.epa.gov, Rtk Chem@EPA
cc:
Subject: HPV Robust Summaries/Test Plan

For the HPV Program, attached in Word format are the test plan and robust summaries for Phosphonic acid, [[bis(2-hydroxyethyl) amino]methyl]-, diethyl ester,
CAS# 2781-11-5, submitted by Akzo Nobel Functional Chemicals LLC. The commitment letter to the HPV Program is dated 3/12/99. The Internal Agency Tracking Numbers on the EPA website are 201-01416 and 201-14323. Bill Gentit of Akzo Nobel Functional Chemicals LLC is the technical contact. He can be reached at 914-674-5394 or by email at william.gentit@akzonobel-chemicals.com. Thanks.

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201-14938A

Fyrol 6
HPV TEST PLAN

Submitted to the U.S. Environmental Protection Agency

By

Akzo Nobel Functional Chemicals LLC

December 2003

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SUMMARY

Akzo Nobel Functional Chemicals LLC has sponsored phosphonic acid, [[bis (2-hydroxyethyl) amino] methyl]- diethyl ester (CAS# 2781-11-5), also known as Fyrol 6, in the U.S. EPA High Production Volume (HPV) program.

Robust summaries of studies on Fyrol 6 are included in this submission. The table below summarizes the endpoints of interest in the HPV program, the available data, and indicates proposed testing.

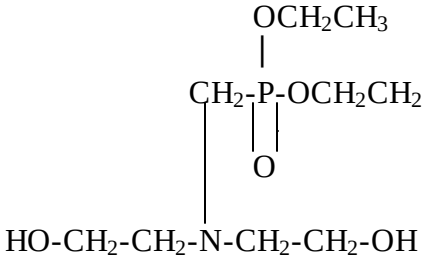
Endpoint	Data Available & Sufficient	Testing Proposed
Physical/Chemical Characteristics		
Melting Point	No	Yes
Boiling Point	Yes	No
Vapor Pressure	Yes	No
Water Solubility	Yes	No
Octanol:Water Partition Coefficient	Yes	No
Photodegradation	Yes	No
Hydrolysis	No	Yes
Biodegradation	Yes	No
Transport	Yes	No
Acute Fish Toxicity	Yes	No
Acute Daphnia Toxicity	No	Yes
Acute Alga Inhibition	No	Yes
Acute Toxicity	Yes	No
Genetic Toxicity	Yes	No
Repeated Dose	Yes	No
Reproductive Toxicity	No	Yes (OECD 421)
Developmental Toxicity	No	Yes (OECD 421)

1.0 INTRODUCTION

Akzo Nobel Functional Chemicals LLC has sponsored phosphonic acid, [[bis (2-hydroxyethyl) amino] methyl]- diethyl ester (CAS# 2781-11-5), also known as Fyrol 6, in the U.S. EPA High Production Volume (HPV) program. Fyrol 6 is a flame retardant that is reacted into rigid polyurethane foam.

This document includes an evaluation of the available toxicity data and test plan. It is proposed that a melting point study, hydrolysis study, acute aquatic invertebrate and algae studies as well as a reproductive/developmental toxicity screening study (OECD 421) be conducted.

Fyrol 6



2.0 USE AND EXPOSURE

Fyrol 6 is manufactured at one site in a closed system in which worker exposure is limited to sampling, analysis in the laboratory and drumming operations. Shipments are typically done in 55 gallon drums and occasionally in bulk tank trucks. Disposal of Fyrol 6 at the manufacturing site is done in a closed wastewater treatment system. Fyrol 6 is used primarily as a flame retardant for urethane and electronic laminate resin systems. Handling by the customer is done via a closed system metered into the resin system during manufacture. Fyrol 6 reacts with and becomes an integral part of the resin system during production. Any worker exposure at the customer's site is during sampling and opening of product containers before processing. Disposal is typically carried out by washing and wastewater treatment.

3.0 EVALUATION OF EXISTING DATA AND PROPOSED TESTING

The available data for Fyrol 6 have been evaluated below and summarized in Tables 1-3. Robust summaries of the studies are included in this submission. The Klimisch reliability code was used in the robust summaries. A literature search on Fyrol 6 of online data bases including TOXLINE, HSDB and RTECS was conducted. There were no relevant studies identified. Fyrol 6 is an amine phosphorous chemical for which there are no structural analogs.

Physical/Chemical Properties:

The melting point for Fyrol 6 is estimated by the EPIWIN model to be 83.21°C. Fyrol 6 is a liquid so the estimation is inaccurate. The boiling point using the EPIWIN model for Fyrol 6 is 379.37°C. The vapor pressure of Fyrol 6 is 0.43 mmHg at 20°C. The log octanol:water partition coefficient (log Kow) of Fyrol 6 is –0.72. The water solubility of Fyrol 6 is 900 g/L.

Recommendation: Testing for melting point is proposed.

Environmental Fate:

AOPWIN was used to estimate the chemical half-life based on an overall OH reaction rate constant. Photodegradation modeling results for Fyrol 6 indicate the half-life is estimated to be 0.898 hours.

Hydrolysis data are not available.

The EPIWIN Level III fugacity model was used to estimate the distribution of Fyrol 6. The modeling results indicate that Fyrol 6 primarily distributes to water and soil.

Fyrol 6 was biodegraded 19% at day 28 of a Modified Sturm Test. It is considered not readily biodegradable.

Recommendation: Testing for hydrolysis is proposed.

Aquatic Toxicity:

The 96 hour LC50 in fish for Fyrol 6 is greater than 10000 mg/L.

Recommendation: Acute testing in Daphnia magna and algae are proposed.

Acute Toxicity:

The acute oral and dermal LD50 values in rats and rabbits for Fyrol 6 are greater than 5000 and 2000 mg/kg, respectively. Fyrol 6 was not irritating to rabbit skin following a 4 hour exposure. It was mildly irritating to rabbits in an eye irritation study.

Recommendation: No additional testing is proposed.

Repeated Dose:
The NOAEL for Fyrol 6 in a 13 week oral gavage study in rats was 500 mg/kg/day. Minor histopathological changes in the liver were seen at 100 and 500 mg/kg/day. The authors of the report suggested that this effect was due to an adaptive response and not the test article.

Recommendation: No additional testing is proposed.

Reproductive/Developmental Toxicity:

There have been no reproductive or developmental toxicity studies conducted on Fyrol 6.

Recommendation: A reproductive/teratology screening study (OECD 421) is proposed for Fyrol 6.

Mutagenicity:
Fyrol 6 was not mutagenic in the Ames test and was negative in the BALB/3T3 cell transformation assay. Fyrol 6 was mutagenic in the mouse lymphoma forward mutation assay and was clastogenic in the mouse lymphoma chromosome aberration study.

Recommendation: No additional testing is proposed.

TABLE 1: PHYSICAL/CHEMICAL DATA

CAS #	Chemical (Mol. Weight)	MW	MP °C	BP °C	Vapor pressure (mmHg)	Water Sol. (g/L)	Log Kow	Phys. Appear.
2781-11-5	Fyrol 6 (255)	216	Test	379.37[a]	0.43	900	-0.72	Clear amber liquid

[a] Data from EPIWIN

TABLE 2: SUMMARY OF ENVIRONMENTAL FATE AND ECOTOXICITY DATA

CAS #	Chemical (Mol. Weight)	Environmental Fate				Ecotoxicity LC50/EC50 (mg/L)		
		Photodeg (hr.).	Stability in water (25°C)	Biodeg.	Trans./ Distr.	Fish	Invert.	Plants
2781-11-5	Fyrol 6 (255)	0.898[a]	Test	Not readily biodegradable	Primarily to soil/water[a]	> 10,000	Test	Test

[a] Data from EPIWIN

TABLE 3: SUMMARY OF MAMMALIAN TOXICITY DATA

CAS #	Chemical (Mol. Weight)					Genetic toxicty	
		Acute (g/kg)	Repeated dose	Reproductive	Develop.	Mutagen.	Chrom. Aberr.
2781-11-5	Fyrol 6 (255)	>5 (oral) >2 (dermal)	NOAEL – 500 mg/kg/day (13 week)	Test (OECD 421)	Test (OECD 421)	Ames- not mutagenic ; Transformation assay – negative ; Mouse lymph. - mutagenic	Mouse lymph. - clastogenic

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201-14938B

Fyrol 6
HPV Robust Summaries
Akzo Nobel Functional Chemicals LLC
December 2003

1. Substance Information

CAS Number:	2781-11-5
Chemical Name:	Phosphonic acid, [[bis (2-hydroxyethyl) amino] methyl]-diethyl ester
Structural Formula:	$C_9H_{22}NO_5P$
Other Names:	Diethyl [(diethanolamino) methyl] phosphonate; Fyrol 6
Exposure Limits:	None

2. Physical – Chemical Properties

2.1. Melting Point:

Identity:	Fyrol 6; CAS# 2781-11-5
Method:	EPIWIN Computer Model
GLP:	Not applicable
Year:	Not applicable
Value:	83.21°C
Decomposition:	Not available
Conclusions:	The melting point of Fyrol 6 is estimated to be 83.21°C.
Reliability:	4
Reference:	1
Remarks:	Fyrol 6 is a liquid but this estimation indicates that it will be a solid. A melting point study should be conducted.
Additional References for Melting Point Studies:	None

2.2. Boiling Point:

Identity:	Fyrol 6; CAS# 2781-11-5
Method:	EPIWIN Computer Model
GLP:	Not applicable
Year:	Not applicable
Value:	379.4°C
Decomposition:	Not available

Conclusions:	The boiling point of Fyrol 6 is estimated to be 379.37°C.
Reliability:	1
Reference:	2
Remarks:	None
Additional References for Melting Point Studies:	None

2.3. Vapor Pressure:

Identity:	Fyrol 6; CAS# 2781-11-5; Lot 0106B-12; purity – 70-90%
Method:	OECD 104
GLP:	No
Year:	2000
Value:	0.43 mm Hg
Temperature° C:	20
Pressure Unit:	MmHg
Decomposition:	Not reported
Conclusions:	The vapor pressure of Fyrol 6 is C is 0.43 mmHg.
Reliability:	2
Reference:	3
Remarks:	Isoteniscope method
Additional Reference for Vapor Pressure Studies:	None

2.4. Partition Coefficient (log Kow):

Identity:	Fyrol 6; CAS# 2781-11-5; Lot 0106B-12; purity – 70-90%
Method:	OECD 107
GLP:	No
Year:	2001
Log Kow:	-0.72
Temperature°C:	25
Conclusions:	The log Kow of Fyrol 6 is -0.72
Reliability:	2
Reference:	4

Remarks:	None
Additional References for Partition Coefficient Studies:	None

2.5. Water Solubility:

Identity:	Fyrol 6; CAS# 2781-11-5; Lot 0106B-12; purity – 70-90%
Method:	OECD 105
GLP:	No
Year:	2001
Value at temperature°C:	900 g/L at 25°C
Description of solubility:	Clear
PH value and concentration at temperature °C:	Not reported
Pka value at 25°C:	Not reported
Conclusions:	The water solubility of Fyrol 6 is 900 g/L.
Reliability:	2
Reference:	5
Remarks:	Flask method
Additional References for Water Solubility Studies:	None

3. Environmental Fate

3.1. Photodegradation:

Identity:	Fyrol 6; CAS# 2781-11-5
Method:	EPIWIN Computer Model
GLP:	Not applicable
Type:	Not applicable
Year:	Not applicable
Light Source:	Not applicable
Light Spectrum (nm):	Not applicable
Half-life:	0.898 hours
Breakdown Products:	Not available
Conclusions:	The half-life in the atmosphere for Fyrol 6 is estimated to be 0.898 hours.
Reliability:	1
Reference:	6
Remarks:	None
Additional References for Photodegradation Studies:	None

3.2. Transport (Fugacity):

Identity:	Fyrol 6; CAS# 2781-11-5			
Method:	EPIWIN Computer Model			
GLP:	Not applicable			
Type:	Not applicable			
Year:	Not applicable			
Media:	Air, Water, Soil, Sediment			
Distributions:	Compartment	Released 100% to air	Release 100% to water	Release 100% to soil
	Air	6.8	3.98×10^{-4}	0.0213
	Water	35	99.8	31.8
	Soil	58.2	3.4×10^{-3}	68.1
	Sediment	0.0645	0.184	0.0681
Conclusions:	Fyrol 6 is distributed primarily to water and soil.			
Reliability:	1			
Reference:	7			
Remarks:	When released equally to air, water and soil, Fyrol 6 is distributed 0.2% to air, 58.3% to water, 41.4% to soil and 0.1% to sediment.			
Additional References for Transport (Fugacity) Studies:	None			

3.3. Biodegradation:

Identity:	Fyrol 6; CAS# 2781-11-5; Batch 8106 J-5-2; purity not given
Method:	OECD 301D
Type:	Modified Sturm Test
GLP:	Yes
Year:	1990
Degradation% after time:	15% (10 mg/L) and 19% (20 mg/L) at 28 days
Breakdown Products:	Not determined
Concentration Of Test Chemical:	10 mg/L, 20 mg/L
pH Of Test Media:	6.87-7.29
Conclusions:	Fyrol 6 is not readily biodegradable.
Reliability:	1
Reference:	8
Remarks:	Source of test organism was activated sludge obtained from a municipal sewage treatment plant
Additional References for Biodegradation Studies:	None

4. Ecotoxicity

4.1. Acute Toxicity to Fish:

Identity:	Fyrol 6; CAS# 2781-11-5; Batch 8106 J-5-2; purity not given
Method:	OECD 203
Type:	Static
GLP:	Yes
Year:	1990
Species/Strain:	Rainbow trout, *salmo gairdneri*
Supplier:	Hauxton Fishery Services, Cambridge, England
Analytical Monitoring:	None
Exposure Period:	96 hours
Nominal Concentrations:	1000, 1800, 3200, 5600 and 10000 mg/L
LC50:	>10000 mg/L
Conclusions:	The LC50 of Fyrol 6 is >10000 mg/L.
Reliability:	1
Reference:	9
Remarks:	There was 20% mortality at 3200 mg/L but none at higher

	concentrations. Ten fish were used in each test group. The water hardness was 216-242 mg/CaCO3/L. The pH was 7.08-8.32. The temperature was 14.1-15.0°C.
Additional References for Acute Toxicity to Fish Studies:	None

5. Mammalian Toxicity

5.1. Acute Toxicity:

5.1.1. Oral

Identity:	Fyrol 6; CAS# 2781-11-5; Lot# 2781115; purity not given
Method:	EPA Guidelines for pesticide registration; Fed. Reg. 43:163, 37336-37402 (1978); OECD (1981)
Type:	Acute Oral LD50
GLP:	Yes
Year:	1983
Species/Strain:	Rat/Sprague-Dawley
Sex:	M/F
No. Of Animals Per Sex Per Dose:	10
Vehicle:	Corn oil
Route Of Administration:	Oral gavage
Time Of Observation Period:	14 Days
Doses Administered:	5000 mg/kg
LD50:	>5000 mg/kg
Conclusions:	The oral LD50 of Fyrol 6 in rats is greater than 5000 mg/kg.
Reliability:	1
Reference:	10
Remarks:	Clinical signs of toxicity were mild depression, piloerection, alopecia and red facial stains. All animals appeared normal by day 2. The only effect seen at necropsy was reddened intestines.
Additional References for Acute Oral Toxicity Studies:	None

5.1.2. Dermal

Identity:	Fyrol 6; CAS# 2781-11-5; Lot# 2781115; purity not given

Method:	EPA Guidelines for pesticide registration; Fed. Reg. 43:163, 37336-37402 (1978); OECD (1981)
Type:	Acute Dermal
GLP:	Yes
Year:	1983
Species/Strain:	Rabbit/Stauffland albino
Sex:	M/F
No. Of Animals Per Sex Per Dose:	5
Vehicle:	None
Route Of Administration:	Dermal
Time Of Observation Period:	14 Days
Doses Administered:	2000 mg/kg for 24 hours
LD50:	>2000 mg/kg
Conclusions:	The dermal LD50 of Fyrol 6 in rabbits is greater than 2000 mg/kg.
Reliability:	1
Reference:	11
Remarks:	There was no mortality. Clinical signs of toxicity were mild depression. All animals appeared normal by day 1. Local dermal effects included mild erythema and edema. There were no adverse effects at necropsy.
Additional References for Acute Dermal Toxicity Studies:	None

5.1.3. Skin Irritation

Identity:	Fyrol 6; CAS# 2781-11-5; Lot# 2781115; purity not given
Method:	DOT Fed. Reg. Title 49, Part 173 Appendix II 10/1/77
Type:	Skin irritation
GLP:	Yes
Year:	1983
Species/Strain:	Rabbit/Stauffland albino
Sex:	M/F
No. Of Animals:	6
Vehicle:	None
Route Of Administration:	Dermal
Time Of Exposure:	4 hours
Time Of	4 and 48 hours

Observation Period:	
Concentration Of Test Material:	0.5mL
Results:	There was no erythema or edema at any observation period. Draize scoring used.
Conclusions:	Fyrol 6 was not irritating to rabbits following dermal exposure for 4 hours.
Reliability:	1
Reference:	12
Remarks:	None
Additional References for Acute Dermal Irritation Studies:	None

5.1.4. Eye Irritation

Identity:	Fyrol 6; CAS# 2781-11-5; Lot# 2781115; purity not given
Method:	EPA Guidelines for pesticide registration; Fed. Reg. 43:163, 37336-37402 (1978); OECD (1981)
Type:	Eye irritation
GLP:	Yes
Year:	1983
Species/Strain:	Rabbit/Stauffland albino
Sex:	M/F
No. Of Animals:	9
Vehicle:	None
Route Of Administration:	Ocular
Time Of Exposure:	Eyes of 3 animals washed after 20-30 seconds of exposure. Eyes of the other 6 animals were not washed.
Time Of Observation Period:	24, 48, 72 hours and 4, 7 days
Concentration Of Test Material:	0.1mL
Results:	There was mild conjunctival irritation in 6 rabbits with unwashed eyes and no effects in the 3 rabbits with washed eyes. The irritation cleared by the 72 hour observation period. Draize scoring used.
Conclusions:	Fyrol 6 was mildly irritating to rabbits.
Reliability:	1
Reference:	13
Remarks:	None

Additional References for Acute Dermal Irritation Studies:	None

5.2. Repeated Dose Toxicity:

Identity:	Fyrol 6; CAS# 2781-11-5; Lot# 1106 L-1; purity – 90.7%
Method:	Repeat Dose - Oral
Type:	13-Week Oral Toxicity
GLP:	Yes
Year:	1983
Species/Strain:	Rat/Sprague-Dawley
Sex:	M/F
No. Of Animals Per Sex Per Dose:	22
Vehicle:	Corn oil
Route of Administration:	Oral gavage
Time of Observation Period:	13 weeks
Doses Administered:	20, 100, 500 mg/kg/day
Frequency of Treatment:	Once daily for 13 weeks, 7 days per week
NOAEL:	500 mg/kg/day
LOAEL:	>500 mg/kg/day
Toxic Response By Dose Level:	Control: Mortality - three females (dosing accident) and three males (dosing accident); Macroscopic exam - enlarged liver in eight animals. 500 mg/kg/day: Mortality – one male (dosing accident) and six females (dosing accident); Clinical signs – alopecia, darker coloration of eyes, chromorhinorrhea; Clinical chemistry – increase in white blood cells; lower hemoglobin and hematocrit; Macroscopic exam – discoloration of lungs, thymus, liver and kidney and enlarged liver; Organ weights – significant increase in mean absolute and relative liver weight and an increase in mean absolute and relative kidney weight; Microscopic exam – very slight hepatocellular hypertrophy, cytoplasmic eosinophilia of centrilobular hepatocytes. 100 mg/kg/day – Mortality – five males (dosing accident) and two females (dosing accident); Clinical signs – alopecia; Clinical

	chemistry – decrease in red blood cells; Macroscopic exam – discoloration of lungs, liver and kidney and enlarged liver; Organ weights – increase in mean relative liver and absolute and relative kidney weight; Microscopic exam – very slight hepatocellular hypertrophy, cytoplasmic eosinophilia of centrilobular hepatocytes. 20 mg/kg/day – Mortality – One male (dosing accident) and three females (dosing accident); Clinical signs – alopecia; Clinical chemistry – decrease in red blood cells; Macroscopic exam – discoloration of lungs and kidney and enlarged liver; Organ weights – no changes; Microscopic exam – no changes. There were no signs of functional changes in the kidney and liver of animals in any dose groups.
Conclusions:	Fyrol 6 administered daily by oral gavage to rats for 13 weeks resulted in minor histopathological changes in the liver at doses of 100 and 500 mg/kg/day. These results were considered an adaptive rather than a toxic response to Fyrol 6. The NOAEL was 500 mg/kg/day.
Reliability:	1
Reference:	14
Remarks:	None
Additional References for Repeated Dose Toxicity Studies:	None

5.3. Genetic Toxicity:

5.3.1. *In Vitro* Gene Mutations

Identity:	Fyrol 6; CAS# 2781-11-5; Lot # 49; purity not given
Method:	Ames test
Type:	Reverse mutation assay
GLP:	Yes
Year:	1978
Cell Type:	Salmonella typhimurium TA1535, TA1537, TA 1538, TA98, TA100; S. cerevisiae D4
Metabolic Activation:	Rat and mouse S9 induced by Aroclor 1254 or phenobarbital
Concentrations Tested:	With/Without S9:0.01-10 ul/plate
Vehicle:	Dimethyl sulfoxide
Cytotoxic Concentration:	No toxicity at any concentration.
Genotoxic Effects With Metabolic Activation:	None

Genotoxic Effects Without Metabolic Activation:	None
Conclusions:	Fyrol 6 was not mutagenic in Salmonella typhimurium strains TA1535, TA1537, TA1538, TA98, TA100 or S. cerevisiae strain D4 in the presence or absence of metabolic activation.
Reliability:	1
Reference:	15
Remarks:	None
Additional References for In Vitro Gene Mutation Studies:	None

Identity:	Fyrol 6; CAS# 2781-11-5; Lot # 49; purity not given
Method:	Mouse lymphoma assay
Type:	Forward mutation assay
GLP:	Yes
Year:	1978
Cell Type:	Mouse lymphoma cell line L5178Y
Metabolic Activation	Rat S9 induced by Aroclor 1254
Concentrations Tested:	With S9: 0.626-2.5 uL/mL Without S9: 1.25-5 ul/mL
Vehicle:	Sterile water
Cytotoxic Concentration:	Cytotoxic at 2.5 and 5 ul/mL
Genotoxic Effects With Metabolic Activation:	Weakly mutagenic
Genotoxic Effects Without Metabolic Activation:	Weakly mutagenic
Conclusions:	Fyrol 6 was weakly mutagenic in the presence and absence of metabolic activation.
Reliability:	1
Reference:	16
Remarks:	None
Additional References for *In Vitro* Mutagenicity Studies:	None

Identity:	Fyrol 6; CAS# 2781-11-5; Lot # 1106C-1-3; purity not given
Method:	Mouse lymphoma assay
Type:	Forward mutation assay
GLP:	Yes
Year:	1981
Cell Type:	Mouse lymphoma cell line L5178Y
Metabolic Activation	Rat S9 induced by Aroclor 1254
Concentrations Tested:	With S9: 0.25-1.0 uL/mL Without S9: 0.0313-0.5 ul/mL
Vehicle:	Sterile water
Cytotoxic Concentration:	Cytotoxic at 0.5 ul/mL
Genotoxic Effects With Metabolic Activation:	Weakly mutagenic
Genotoxic Effects Without Metabolic Activation:	Weakly mutagenic
Conclusions:	Fyrol 6 was weakly mutagenic in the presence and absence of metabolic activation.
Reliability:	1
Reference:	17
Remarks:	None
Additional References for *In Vitro* Mutagenicity Studies:	None

5.3.2. *In Vitro* Chromosome Aberrations

Identity:	Fyrol 6; CAS# 2781-11-5; Lot # 1106C-1-3; purity not given
Method:	Mouse lymphoma assay
Type:	Chromosome aberration
GLP:	Yes
Year:	1982
Cell Type:	Mouse lymphoma cell line L5178Y
Metabolic Activation	Rat S9 induced by Aroclor 1254
Concentrations	With S9: 0.25-2.0 uL/mL

Tested:	Without S9: 0.0313-0.5 ul/mL
Vehicle:	Sterile water
Cytotoxic Concentration:	None
Genotoxic Effects With Metabolic Activation:	Clastogenic. Both structural and numerical chromosome aberrations were seen in the two highest dose groups.
Genotoxic Effects Without Metabolic Activation:	Clastogenic. Both structural and numerical chromosomal aberrations were seen in the two highest dose groups.
Conclusions:	Fyrol 6 was clastogenic in the presence and absence of metabolic activation.
Reliability:	1
Reference:	18
Remarks:	A statistically significant increase in structural and numerical aberrations was reported.
Additional References for *In Vitro* Chromosome Abberration Studies:	None

In Vitro Transformation

Identity:	Fyrol 6; CAS# 2781-11-5; Lot # 49; purity not given
Method:	BALB/3T3 Cell assay
Type:	In vitro transformation assay
GLP:	Yes
Year:	1978
Cell Type:	BALB/3T3 cells
Metabolic Activation	Not applicable
Concentrations Tested:	0.02-0.312 uL/mL
Vehicle:	Medium
Cytotoxic Concentration:	None
Genotoxic Effects With Metabolic Activation:	None
Genotoxic Effects Without Metabolic Activation:	None
Conclusions:	Fyrol 6 was not active in this assay.

Reliability:	1
Reference:	19
Remarks:	The cells were examined after a 72 hour exposure period and 3-4 week growth period
Additional References for *In Vitro* Trans-formation Studies:	None

5.4 Neurotoxicity

Identity:	Fyrol 6; CAS# 2781-11-5; Lot# 0106E-2-2; purity – 97.4%
Method:	Fed. Reg. 43 (163):37362-37363, 1978
Type:	Acute Delayed Neurotoxicity
GLP:	Yes
Year:	1982
Species/Strain:	Hen/White Leghorn
Sex:	F
No. Of Animals Per Sex Per Dose:	10
Vehicle:	Corn oil
Route of Administration:	Oral gavage
Time of Observation Period:	43 Days
Doses Administered:	1 or 10 g/kg
Frequency of Treatment:	Two doses, three weeks apart
NOAEL (NOEL):	10 g/kg x 2
LOAEL (LOEL):	None
Toxic Response By Dose Level:	None
Conclusions:	Fyrol 6 administered to hens did not cause delayed neurotoxicity at doses up to 10 g/kg administered 3 weeks apart.
Reliability:	1
Reference:	20
Remarks:	Tri-ortho-cresyl phosphate was used as the positive control. Clinical and histopathology evaluation was done.
Additional References for Repeated Dose Toxicity Studies:	None

References

1) EPIWIN 3.10 U.S. Environmental Protection Agency 2000

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